Reaction of 2-Aminobenzamide Analogs and 2-Aminothiophenol with Ethyl 3-Ethoxymethylene-2,4-dioxovalerate. Synthesis of Pyrrolo[1,2-*a*]quinazoline and Pyrrolo[1,2-*a*]benzothiazoline Derivatives

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The reaction of ethyl 3-ethoymethylene-2,4-dioxovalerate (EMDV) (**1**) with 2-aminobenzamide (**2**), 2-aminobenzthioamide (**3**), 2-aminobenzmethylamide (**4**) and 3-amino-2-methyl- or phenylpyrazole-4-carboxamides (**6** and **7**) produced ethyl 3-aminomethylene-2,4-dioxovalerates (**10, 15, 16, 18** and **19**), which led to pyrrolo[1,2-*a*]quinazoline-1,5-diones (**11, 22** and **23**) and pyrrolo[1,2-*a*]pyrazolo[4,3-*e*]pyrimidine-1,5-diones (**24** and **25**) under the acidic condition, respectively. Analogously, 2-aminothiophenol reacted with **1** to give **21**, which was subsequently derived to pyrrolo[1,2-*a*]benzothiazolin-1-one (**26**) under the neutral condition. Furthermore, we prepared the heterocyclic steroidal molecules (**41, 43, 45, 47, 49** and **51**) by condensation of **11** and **26** with hydrazine, methylhydrazine and phenylhydrazine.

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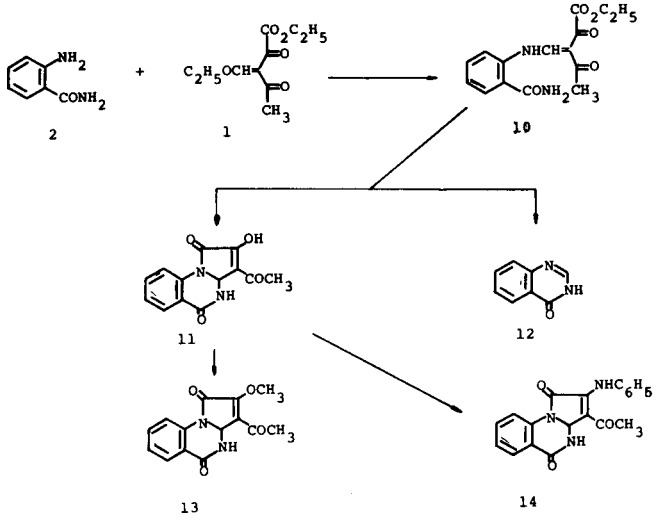
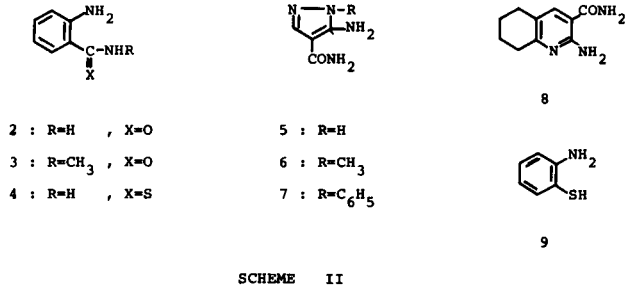
The synthesis of pyrrolo[1,2-*a*]quinazoline-1,5-dione, some of which have the anti-edema activity, have hitherto been reported by some workers (1). Recently, we have reported the reaction of ethyl 3-ethoxymethylene-2,4-dioxovalerate (EMDV) (**1**) with 2-aminobenzamide derivatives (2) or 3-aminopyrazole-4-carboxamides (3) to give pyrrolo[1,2-*a*]quinazoline-1,5-dione or pyrrolo[1,2-*a*]-pyrazolo[4,3-*e*]pyrimidine-1,5-dione derivatives. The present paper describes the reaction of EMDV with several kinds of 2-aminobenzamide analogs or 2-aminothiophenol, involving a full account of previous brief communications (2,3).

Treatment of 2-aminobenzamide (**2**) with an equimolar of EMDV in ethanol under reflux for 4 hours gave a mixture of 3,4-dihydro-4-oxoquinazoline (**12**) and 3-acetyl-3a,4-dihydro-2-hydroxypyrrolo[1,2-*a*]quinazoline-1,5-dione (**11**) in 70% and 12% yield, respectively. Compound **11** is soluble in sodium bicarbonate solution and showed wine-red color when treated with ferric chloride. Structural elucidation of **11** was fully achieved on the basis of its elemental analysis and the data of nuclear magnetic resonance (nmr) (deuteriodimethylsulfoxide) which exhibited a characteristic methine proton (C_{3a}-H) at δ 6.10 as singlet, and the other signals shown in Experimental. Methylation of **11** with diazomethane gave the corresponding methylether (**13**). The enol structure of **11** was further confirmed to derive to 3-acetyl-2-anilino-3a,4-dihydropyrrolo[1,2-*a*]quinazoline-1,5-dione (**14**) by the reaction of **11** with aniline (4). EMDV was, however, treated with **2** in ethanol under ice cooling, ethyl 3-(2-carbamoylanilino)-methylene-2,4-dioxovalerate (**10**) was isolated in 97% yield. The nmr spectrum of **10** exhibited a vinyl proton (=CH) at δ 8.65 as a doublet coupled with NH group. When **10** was then refluxed in ethanol for 3 hours, **11** was obtained in 36% yield. Finally, the yield was optimized to 84.5% by refluxing **10** in ethanol containing a small amount of concentrated hydrochloric acid. To extend this type of double cyclization reaction, **1** was, moreover, reacted with the following compounds [2-aminobenzmethylamide (**3**), 2-aminobenzthioamide (**4**), 3-aminopyrazole-4-carboxamide (**5**), 3-amino-2-methyl- or phenylpyrazole-4-carboxamide (**6** and **7**) (5), 2-amino-5,6,7,8-tetrahydroquinoline-3-carboxamide (**8**) (6), and 2-aminothiophenol (**9**)] to give the corresponding aminomethylene



SCHEME I



SCHEME II

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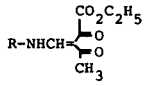
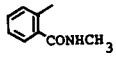
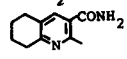
Table I

Physical and Analytical Data for Aminomethylene Derivatives



Compound No.	R	Formula	Analysis (%) Calcd. (Found) C	H	N	Nmr (DMSO-d_6) -NHC*H*= (δ)
10		$C_{15}H_{16}N_2O_5$	59.02 (59.10)	5.30 (5.14)	9.21 (9.18)	8.65 (d, J = 13 Hz)
15		$C_{16}H_{18}N_2O_5$	60.37 (60.54)	5.70 (5.61)	8.80 (8.68)	8.62 (d, J = 13 Hz)
16		$C_{15}H_{16}N_2O_4S$	56.23 (56.42)	5.03 (4.99)	8.75 (8.65)	8.63 (d, J = 13 Hz)
17		$C_{12}H_{14}N_4O_5$	48.98 (48.73)	4.80 (4.70)	19.04 (18.83)	7.79 (d, J = 6 Hz)
18		$C_{13}H_{16}N_4O_5$	50.64 (50.69)	5.23 (5.10)	18.18 (18.17)	8.73 (d, J = 13 Hz)
19		$C_{16}H_{18}N_4O_5$	58.37 (58.37)	4.90 (4.77)	15.13 (15.23)	8.48 (d, J = 13 Hz)
20		$C_{15}H_{21}N_3O_5$	60.10 (60.10)	5.89 (5.75)	11.69 (11.54)	(a)
21		$C_{14}H_{15}NO_4S$	57.32 (57.52)	5.15 (4.97)	4.78 (4.87)	8.64 (d, J = 13 Hz)

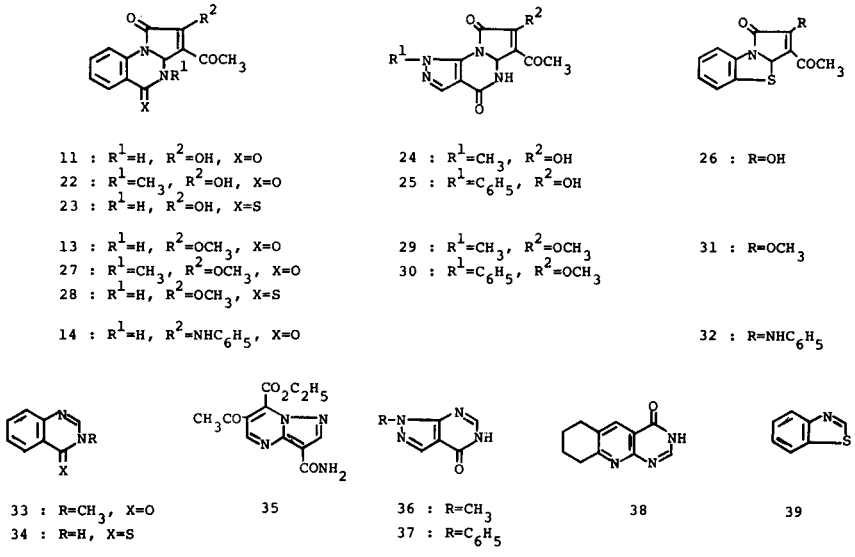
(a) Fine spectrum was not obtained because of insolubility.

Table II

Physical and Analytical Data of Tricyclic Enols

Compound No.	M.p. °C (Recrystallization Solvent)	Formula	Analysis (%) Calcd. (Found) C	H	N
11	268-270 (DMF)	$C_{13}H_{10}N_2O_4$	60.46 (60.22)	3.90 (3.75)	10.85 (10.95)
22	231-232 (methanol)	$C_{14}H_{12}N_2O_4$	61.76 (61.82)	4.44 (4.35)	10.29 (10.12)
23	227-228 (methanol)	$C_{13}H_{10}N_2O_3S$	56.92 (57.14)	3.67 (3.87)	10.22 (10.41)
24	268-269 (methanol)	$C_{11}H_{10}N_4O_4$	50.38 (50.38)	3.84 (3.80)	21.37 (21.25)
25	254-255 (methanol)	$C_{16}H_{12}N_4O_4$	59.26 (59.36)	3.73 (3.91)	17.28 (17.22)
26	164-166 (ethanol)	$C_{12}H_9NO_3S$	58.30 (58.49)	3.67 (3.60)	5.67 (5.77)

derivatives (**10, 15-21**) (Table I) in ethanol or ether under ice cooling in moderate yield. As in the case of **10**, compound **15** and **16** were refluxed in ethanol-hydrochloric acid to give pyrrolo[1,2-*a*]quinazoline-1,5-diones (**22** and **23**), together with quinazolones (**33** and **34**). In the cases of compound **18** and **19**, the best results were obtained by refluxing in acetic acid to give pyrrolo[1,2-*a*]pyrazolo-[4,3-*e*]pyrimidine-1,5-diones (**24** and **25**), together with pyrazolopyrimidones (**36** and **37**) (5), but the yields were not so good. It is interesting to note that compound **17**, having no substituent on pyrazole ring nitrogen, was refluxed in ethanol for 5 minutes to furnish 6-acetyl-7-



SCHEME III

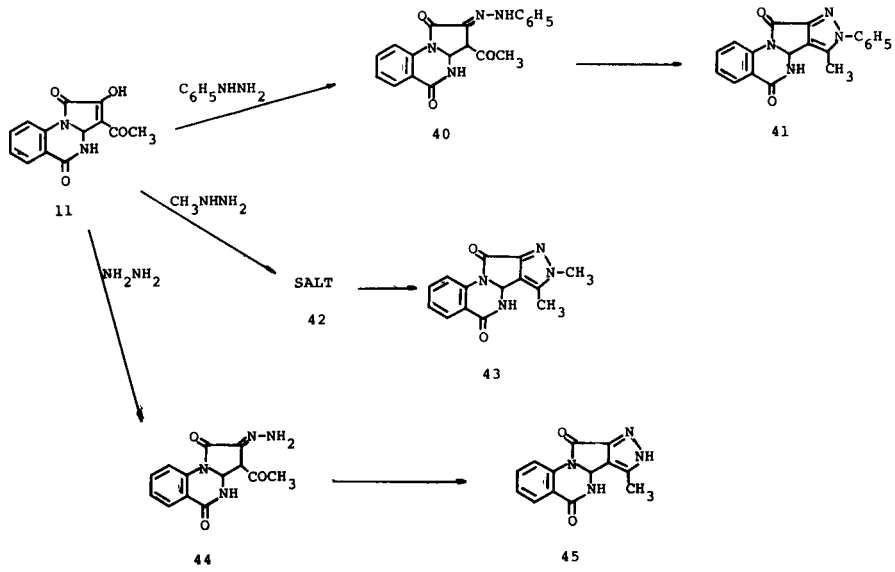
carbethoxypyrazolo[1,5-*a*]pyrimidine-3-carboxamide (**35**) in a quantitative yield, whose structural assignment was based on its elemental analysis and spectral data (3). In our analogous reaction condition, an attempt to obtain the double cyclized product from **20** was unsuccessful, resulting merely in bond fission to give **38** in 82% yield. Finally, the thiol **21** was cyclized to 3-acetyl-2-hydroxypyrrolo[1,2-*a*]benzothiazolin-1-one (**26**) by refluxing in ethanol in 51% yield, together with benzothiazole (**39**). In this case, the addition of hydrochloric acid did not give the satisfactory result for the increase of the yield of **26**, but the unidentified material, m.p. 233-234°, was isolated in low yield. Treatment of **26** with aniline afforded anilide (**32**). All of the tricyclic enol derivatives (**11, 22-26**) (Table II) were derived to the methyl ethers (**13, 27-31**) by treatment with diazomethane, and the physical and analytical data were summarized in Table III.

Next, we attempted to prepare the heterocyclic steroidal molecules by the condensation of the representative tricyclic compounds (**11** and **26**) with hydrazine derivatives. Condensation of **11** or **26** with phenylhydrazine gave the corresponding phenylhydrazones, which are shown in Schemes IV and V. Whereas the hydrazone derived from **26** exists in the enehydrazine structure (**46**) (7), the product obtained from **11** was found to be the tautomeric hydrazone form (**40**) from the nmr spectral study. The

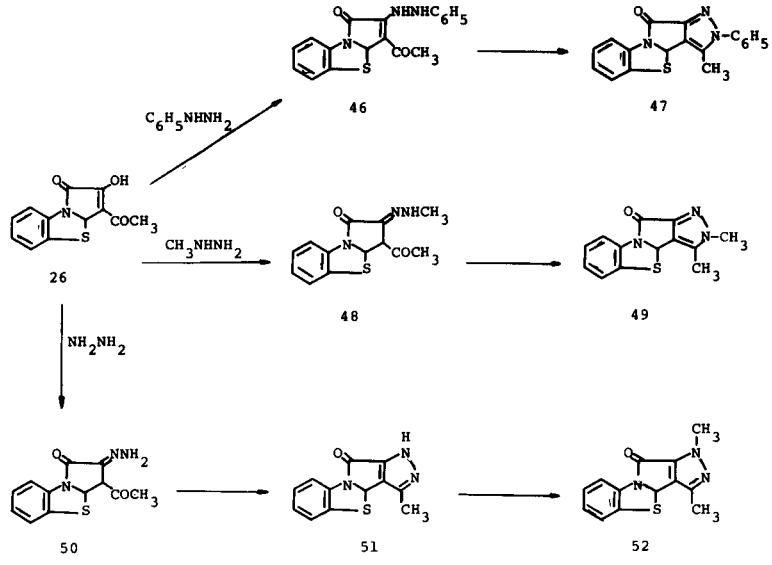
Table III

Physical and Analytical Data of Tricyclic Methylethers

Compound No.	M.p. °C (Recrystallization Solvent)	Formula	Analysis (%) Calcd. (Found) C	H	N
13	188-190 (ethanol)	$C_{14}H_{12}N_2O_4$	61.76	4.44	10.29
			(61.66)	(4.35)	(10.11)
27	231-232 (methanol)	$C_{15}H_{14}N_2O_4$	62.93	4.93	9.79
			(63.14)	(4.78)	(9.62)
28	161-162 (ethanol)	$C_{14}H_{12}N_2O_3S$	58.33	4.20	9.72
			(58.41)	(4.27)	(9.80)
29	200-202 (methanol)	$C_{12}H_{12}N_4O_4$	52.17	4.38	20.28
			(52.44)	(4.37)	(20.55)
30	227-228 (ethanol)	$C_{17}H_{14}N_4O_4$	60.35	4.17	16.56
			(60.39)	(4.18)	(16.70)
31	159-160 (ethanol)	$C_{13}H_{11}NO_3S$	59.75	4.24	5.36
			(59.58)	(4.36)	(5.45)



SCHEME IV



SCHEME V

heterocyclic ring protons at position 3 and 3a are seen as one-proton doublets (J = 3 Hz) at δ 3.75 and δ 5.45, respectively. In contrast, the nmr spectrum of **46** showed a one-proton singlet at δ 6.67 for the heterocyclic ring proton at position 3a. Heating of **40** in ethanol-hydrochloric acid or **46** in ethyl cellosolve-hydrochloric acid effected their cyclization to give 3-methyl-2-phenyl-3b,4-dihydropyrazolo[4,3-*c*]quinazolo[1,2-*a*]pyrrole-5,11-dione (**41**) or 3-methyl-2-phenylpyrazolo[4,3-*c*]benzothiazolino[1,2-*a*]-pyrrol-10-one (**47**).

Reaction of **11** with methylhydrazine in ethanol at room temperature afforded the corresponding salt (**42**), which was then refluxed in ethanol to give 2,3-dimethyl-3b,4-dihydropyrazolo[4,3-*c*]quinazolo[1,2-*a*]pyrrole-5,11-dione (**43**). On the other hand, when 26 was treated with methylhydrazine in refluxing ethanol, methylhydrazone (**48**) which exhibited one-proton doublets (J = 5 Hz) at δ 3.90 and δ 5.77 due to the heterocyclic ring protons at position 3 and 3a, was isolated. By prolonged heating in ethanol with the addition of hydrochloric acid, cyclization was brought to completion, and 2,3-dimethylpyrazolo[4,3-*c*]-benzothiazolino[1,2-*a*]pyrrol-10-one (**49**) was obtained.

Finally, **11** and **26** were treated with hydrazine hydrate in refluxing ethanol to give the hydrazones (**44** and **50**), which were subsequently refluxed for extended periods of time with the addition of hydrochloric acid in ethanol or ethyl cellosolve, and the tetracyclic compounds (**45** and **51**) were obtained. Methylation of **51** with methyliodide in the

presence of potassium carbonate in acetone afforded 1,3-dimethylpyrazolo[4,3-*c*]benzothiazolino[1,2-*a*]pyrrol-10-one (**52**), which is the isomer of compound **49**.

EXPERIMENTAL

All melting points were not corrected. Infrared and ultra violet spectra were taken on a JASCO IRA-1 and Schimadzu UV-200 spectrophotometers. Nmr spectra were determined for solution of deuteriodimethylsulfoxide with TMS as the internal standard with Hitachi R-40 spectrometer.

General Preparation of Ethyl 3-Aminomethylene-2,4-dioxovalerates (**10**, **15-21**).

To a solution of aminocarboxamides (**2-9**) (0.01 mole) in ethanol (30 ml.) (ether in cases of **2** and **9**), **1** (0.01 mole) dissolved in ethanol (or ether) (20 ml.) was added with stirring under ice cooling. The precipitate formed was collected by filtration, washed with cold solvent, and dried (Table I).

Ethyl 3-(2-Carbamoylanilino)methylene-2,4-dioxovalerate (**10**).

This compound had m.p. 163-164° (without recrystallization), colorless powder, yield 97%.

Ethyl 3-(2-*N*-Methylcarbamoylanilino)methylene-2,4-dioxovalerate (**15**).

This compound had m.p. 139-140° (without recrystallization), colorless powder, yield 96%.

Ethyl 3-(2-Thiocarbamoylanilino)methylene-2,4-dioxovalerate (**16**).

This compound had m.p. 289-290° (without recrystallization), yellow powder, yield 96%.

Ethyl 3-(4-Carbamoyl-3-pyrazoloamino)methylene-2,4-dioxovalerate (**17**).

This compound had m.p. 146-147° (without recrystallization), colorless powder, yield 94%.

Ethyl 3-(4-Carbamoyl-2-methyl-3-pyrazoloamino)methylene-2,4-dioxovalerate (**18**).

This compound had m.p. 163-165° (ethanol), colorless needles, yield 92%.

Ethyl 3-(4-Carbamoyl-2-phenyl-3-pyrazoloamino)methylene-2,4-dioxovalerate (**19**).

This compound had m.p. 174-175° (ethanol), colorless needles, yield 96%.

Ethyl 3-(3-Carbamoyl-5,6,7,8-tetrahydro-2-quinolylamino)methylene-2,4-dioxovalerate (**20**).

This compound had m.p. 222-223° (without recrystallization), colorless powder, yield 99%.

Ethyl 3-(2-Mercaptoanilino)methylene-2,4-dioxovalerate (**21**).

This compound had m.p. 138-140° (without recrystallization), yellow powder, yield 95%.

3-Acetyl-3a,4-dihydro-2-hydroxypyrrolo[1,2-*a*]quinazoline-1,5-dione (**11**).

A mixture of 1 g. of **10**, two drops of concentrated hydrochloric acid and 80 ml. of ethanol was refluxed for 3 hours. The deposited solid was collected by filtration, washed with cold ethanol, and dried, yielding 0.678 g. of **11** as colorless prisms. The filtrate was condensed to a small volume and the resulting solid was collected by filtration, yielding 0.025 g. of **11**. Total yield was 0.703 g. (84.5%); ir (potassium bromide): ν max cm^{-1} 3400, 3280, 1710, 1630; nmr: δ 2.45 (3H, s, $COCH_3$), 6.10 (1H, s, CH), 7.30-8.10 (4H, m, Ar-H), 8.30 (1H, s, NH). The filtrate was condensed to dryness *in vacuo*, and the resulting solid was recrystallized from ethanol to give 3,4-dihydro-4-oxoquinazoline (**12**), m.p. 210-212° [lit. (8) m.p. 211-212°].

3-Acetyl-3a,4-dihydro-2-hydroxy-4-methylpyrrolo[1,2-*a*]quinazoline-1,5-dione (**22**).

A mixture of 4.54 g. of **15**, three drops of concentrated hydrochloric acid and 200 ml. of ethanol was refluxed for 3 hours. The solvent was evaporated *in vacuo*, and the resulting solid was recrystallized from ethanol to give 2.2 g. (52%) of **22** as colorless needles; ir (potassium bromide): ν max cm^{-1} 3400, 1710, 1650; uv (ethanol): λ max nm (log ϵ) 246 (4.25), 304 (3.95), 327 (3.81); nmr: δ 2.43 (3H, s, $COCH_3$), 2.93 (3H, s, NCH_3), 6.13 (1H, s, CH), 7.30-8.10 (4H, m, Ar-H), 11.0 (1H, bs, NH). The filtrate was condensed *in vacuo*, and the residue was recrystallized from ligroin to give 3,4-dihydro-3-methyl-4-oxoquinazoline (**33**), m.p. 101-102° [lit. (9) m.p. 100-101°].

3-Acetyl-3a,4-dihydro-2-hydroxy-5-thiocarbonylpyrrolo[1,2-*a*]quinazoline-1-one (**23**).

A mixture of 5.8 g. of **16**, three drops of concentrated hydrochloric acid and 60 ml. of ethanol was refluxed for 1.5 hours. Evaporation of the solvent *in vacuo* left a yellow solid, which was dissolved in saturated sodium bicarbonate solution. The insoluble solid was collected by filtration, and recrystallized from ethanol to give thioquinazolone (**34**), m.p. > 300° [lit. (10), m.p. 324-325°]. Acidification of the aqueous filtrate by the addition of 10% hydrochloric acid precipitated 1.74 g. (35%) of **23**, which was recrystallized from ethanol to give analytical sample as yellow needles; ir (potassium bromide): ν max cm^{-1} 3400, 3280, 1715, 1650; uv (ethanol): λ max nm (log ϵ) 265 (4.20), 321 (4.09); nmr: δ 2.40 (3H, s, $COCH_3$), 5.93 (1H, s, CH), 7.20-8.30 (4H, m, Ar-H), 10.50 (1H, s, NH), 11.80 (1H, bs, OH).

3-Acetyl-3a,4-dihydro-2-hydroxy-8-methylpyrrolo[1,2-*a*]pyrazolo[4,3-*e*]-pyrimidine (**24**).

A solution of 2 g. of **18** in 50 ml. of acetic acid was refluxed for 3 hours. After evaporation of the solvent, the residue was dissolved in saturated sodium bicarbonate solution. The insoluble solid was collected by filtration, recrystallized from ethanol to give 1-methyl-4-hydoxypyrazolo-[3,4-*d*]pyrimidine (**36**), m.p. > 300° [lit. (5) m.p. > 300°]. Acidification of the aqueous filtrate by the addition of 10% hydrochloric acid precipitated 0.227 g. (12.4%) of **24**, which was recrystallized from methanol to give an analytical sample as colorless needles; ir (potassium bromide): ν max cm^{-1} 3380, 1725, 1630; nmr: δ 2.45 (3H, s, $COCH_3$), 4.00 (3H, s, NCH_3), 6.10 (1H, s, CH), 7.70 (1H, s, NH), 7.85 (1H, s, Ar-H).

3-Acetyl-3a,4-dihydro-2-hydroxy-8-phenylpyrrolo[1,2-*a*]pyrazolo[4,3-*e*]-pyrimidine (**25**).

A solution of 3 g. of **19** in 50 ml. of acetic acid was refuxed for 3 hours. After evaporation of the solvent, the residue was dissolved in saturated sodium bicarbonate solution. The insoluble solid was collected by filtration, recrystallized from ethanol to give 1-phenyl-4-hydroxypyrazolo-[3,4-*d*]pyrimidine (**37**), m.p. 301-302° (lit. (5) m.p. 299°). Acidification of the aqueous filtrate by the addition of 10% hydrochloric acid precipitated 1.12 g. (42.6%) of **25**, which was recrystallized from methanol to give an analytical sample as colorless needles; ir (potassium bromide): ν max cm^{-1} 3380, 1725, 1630; nmr: δ 2.40 (3H, s, $COCH_3$), 6.25 (1H, s, CH), 7.80 (1H, s, NH), 8.05 (1H, s, Ar-H).

3-Acetyl 2-hydroxypyrrolo[1,2-*a*]benzothiazolin-1-one (**26**).

A solution of 28 g. of **21** in 300 ml. of ethanol was refluxed for 4 hours. Evaporation of the solvent *in vacuo* left a yellow semisolid, which was dissolved in saturated sodium bicarbonate solution. The insoluble oil was extracted with chloroform. The extract was dried (sodium sulfate) and evaporated to give an oily residue, which was identical with the commercial benzothiazole by comparison of their ir spectra. Acidification of the aqueous phase by the addition of 10% hydrochloric acid precipitated 12 g. (52%) of **26**, which was recrystallized from ethanol to give an analytical sample as yellow needles; ir (potassium bromide): ν max cm^{-1} 3600-3400, 1710, 1630; nmr: δ 2.47 (3H, s, $COCH_3$), 6.73 (1H, s, CH), 7.1-7.6 (4H, m, Ar-H), 11.0 (1H, bs, OH).

General Preparation of Methylethers (**13**, **27-31**).

To ethereal solution including a large excess of diazomethane was added the enols (**11**, **22-26**), and the suspended mixture was stirred overnight. The precipitate was collected by filtration, and recrystallized to give the methylethers (Table III) in 90-95% yield.

3-Acetyl-3a,4-dihydro-2-methoxypyrrolo[1,2-*a*]quinazoline-1,5-dione (**13**).

This compound had ir (potassium bromide): ν max cm^{-1} 3280, 1720, 1680, 1650; nmr: δ 2.43 (3H, s, $COCH_3$), 4.38 (3H, s, OCH_3), 6.13 (1H, s, CH), 8.43 (1H, s, NH).

3-Acetyl-3a,4-dihydro-2-methoxy-4-methylpyrrolo[1,2-*a*]quinazoline-1,5-dione (**27**).

This compound had ir (potassium bromide): ν max cm^{-1} 1720, 1680, 1650; nmr: δ 2.53 (3H, s, $COCH_3$), 2.90 (3H, s, NCH_3), 4.40 (3H, s, OCH_3), 6.18 (1H, s, CH).

3-Acetyl-3a,4-dihydro-2-methoxy-5-thiocarbonylpyrrolo[1,2-*a*]quinazolin-1-one (**28**).

This compound had ir (potassium bromide): ν max cm^{-1} 1720, 1670, 1620; nmr: δ 2.40 (3H, s, $COCH_3$), 4.45 (3H, s, OCH_3), 6.00 (1H, s, CH), 10.73 (1H, bs, NH).

3-Acetyl-3a,4-dihydro-2-methoxy-8-methylpyrrolo[1,2-*a*]pyrazolo[4,3-*e*]-pyrimidine (**29**).

This compound had ir (potassium bromide): ν max cm^{-1} 1750, 1730, 1670, 1630; nmr: δ 2.43 (3H, s, $COCH_3$), 3.97 (3H, s, NCH_3), 4.35 (3H, s, OCH_3), 6.10 (1H, s, CH), 7.80 (1H, s, NH), 7.87 (1H, s, Ar-H).

3-Acetyl-3a,4-dihydro-2-methoxy-8-phenylpyrrolo[1,2-*a*]pyrazolo[4,3-*e*]-pyrimidine (**30**).

This compound had ir (potassium bromide): ν max cm^{-1} 1740, 1670, 1630; nmr: δ 2.40 (3H, s, $COCH_3$), 4.10 (3H, s, OCH_3), 6.25 (1H, s, CH), 7.93 (1H, s, NH), 8.03 (1H, s, Ar-H).

3-Acetyl-2-methoxypyrrolo[1,2-*a*]benzothiazolin-1-one (**31**).

This compound had ir (potassium bromide): ν max cm^{-1} 1720, 1650, 1610; nmr: δ 2.43 (3H, s, $COCH_3$), 4.30 (3H, s, OCH_3), 6.60 (1H, s, CH).

3-Acetyl-2-anilino-3a,4-dihydropyrrolo[1,2-*a*]quinazoline-1,5-dione (**14**).

A mixture of 0.3 g. of **11**, 0.109 g. of aniline and 50 ml. of dimethylformamide was refluxed for 5 hours. After evaporation of the solvent *in vacuo*, the crystalline residue was recrystallized from acetonitrile to give 0.174 g. (45%) of **14** as yellow needles of m.p. 292-294°; ir (potassium bromide): ν max cm^{-1} 3280, 1720, 1670, 1640; nmr: δ 2.33 (3H, s, $COCH_3$), 6.30 (1H, s, CH), 9.03 and 11.40 (each 1H, each s, 2 × NH).

Anal. Calcd. for $C_{19}H_{15}N_3O_3$: C, 68.46; H, 4.54; N, 12.61. Found: C, 68.53; H, 4.48; N, 12.81.

3-Acetyl-2-anilinopyrrolo[1,2-*a*]benzothiazolin-1-one (**32**).

A mixture of 0.247 g. of **26**, 0.093 g. of aniline, and 30 ml. of ethanol was refluxed for 6 hours. After evaporation of the solvent the resulting yellow solid was recrystallized from benzene to yield 0.18 g. (55.8%) of **32** as yellow needles of m.p. 217-218°; ir (potassium bromide): ν max cm^{-1} 1720, 1630; nmr: δ 2.27 (3H, s, $COCH_3$), 7.04 (1H, s, CH), 7.1-7.7 (9H, m, Ar-H), 12.35 (1H, bs, NH).

Anal. Calcd. for $C_{18}H_{14}N_2O_2S$: C, 67.07; H, 4.38; N, 8.96. Found: C, 67.14; H, 4.31; N, 8.84.

6-Acetyl-7-carbethoxypyrazolo[1,5-*a*]pyrimidine-3-carboxamide (**35**).

A solution of 29.4 g. of **17** in 200 ml. of ethanol was refluxed for 5 minutes. After cooling, the precipitate was collected by filtration, washed with cold ethanol, and dried to give 27.5 g. (100%) of **35**. Recrystallization from ethanol afforded an analytical sample as colorless needles of m.p. 202-204°; ir (potassium bromide): ν max cm^{-1} 3400, 1760, 1695, 1660; uv (ethanol): λ max nm (log ϵ) 257 (4.40), 312 (3.90); nmr: δ 1.40 (3H, t, J = 6 Hz, CH_2CH_3), 2.76 (3H, s, $COCH_3$), 4.56 (2H, q, J = 6 Hz, CH_2CH_3), 7.50 and 7.70 (each 1H, each bs, NH_2), 8.30 (1H, s, C_2-H), 9.50 (1H, s, C_5-H).

Anal. Calcd. for $C_{12}H_{12}N_4O_4$: C, 52.17; H, 4.38; N, 20.28. Found: C, 52.32; H, 4.29; N, 20.16.

4-Hydroxy-6,7,8,9-tetrahydropyrimido[4,5-*b*]quinoline (**38**).

A solution of 0.3 g. of **20** in 20 ml. of ethyl cellosolve was refluxed for 2 hours and condensed to a small volume. After cooling the precipitate was collected by filtration to give 0.138 g. (82%) of **38**. Recrystallization from ethyl cellosolve afforded an analytical sample as colorless needles of m.p. > 300°; ir (potassium bromide): ν max cm^{-1} 1685.

Anal. Calcd. for $C_{11}H_{11}N_3O$: C, 65.67; H, 5.51; N, 20.88. Found: C, 65.78; H, 5.54; N, 20.74.

3-Acetyl-3a,4-dihydro-1,2,5-trioxopyrrolidino[1,2-*a*]quinazoline Phenylhydrazone (**40**).

A mixture of 1.0 g. of **11**, 0.45 g. of phenylhydrazine, and 200 ml. of ethanol was refluxed for 9 hours. The solvent was condensed to a small volume, and the resulting precipitate was collected by filtration. Recrystallization from ethanol afforded 1.16 g. (86%) of **40** as colorless needles of m.p. > 300°; ir (potassium bromide): ν max cm^{-1} 1720, 1670, 1600; nmr: δ 2.13 (3H, s, $COCH_3$), 3.75 and 5.45 (each 1H, each d, J = 3 Hz, C_3- and C_{3a}-H).

Anal. Calcd. for $C_{19}H_{16}N_4O_3$: C, 65.61; H, 4.63; N, 16.08. Found: C, 65.66; H, 4.77; N, 16.21.

3-Methyl-2-phenyl-3b,4-dihydropyrazolo[4,3-*c*]quinazolo[1,2-*a*]pyrrole-5,11-dione (**41**).

A solution of 0.4 g. of **40** in 30 ml. of ethyl cellosolve with the addition of two drops of concentrated hydrochloric acid was refluxed for 1 hour. After cooling the precipitate was collected by filtration, recrystallized from dimethylformamide to give 0.21 g. (74%) of **41** as colorless needles of m.p. > 300°; ir (potassium bromide): ν max cm^{-1} 1720, 1670; nmr: δ 2.46 (3H, s, CH_3), 6.50 (1H, s, CH).

Anal. Calcd. for $C_{19}H_{14}N_4O_2$: C, 69.08; H, 4.27; N, 16.96. Found: C, 69.03; H, 4.25; N, 16.97.

Methylhydrazine Salt (**42**) of **11**.

To a suspended solution of 0.5 g. of **11** in 25 ml. of ethanol was added 0.15 g. of methylhydrazine dissolved in 5 ml. of ethanol, and the mixture was stirred for 3 hours. The resulting salt was collected by filtration, washed with cold ethanol, and dried to give 0.55 g. (94%) of **42** as colorless powder of m.p. 273-275°; ir (potassium bromide): ν max cm^{-1} 1720, 1680, 1640.

Anal. Calcd. for $C_{14}H_{16}N_4O_4$: C, 55.25; H, 5.30; N, 18.41. Found: C, 55.05; H, 5.13; N, 18.38.

2,3-Dimethyl-3b,4-dihydropyrazolo[4,3-*c*]quinazolo[1,2-*a*]pyrrole-5,11-dione (**43**).

A solution of 0.5 g. of **42** dissolved in 50 ml. of ethanol was refluxed for 24 hours. After cooling the precipitate was collected by filtration, and recrystallized from methanol to give 0.206 g. (47%) of **43** as colorless needles of m.p. > 300°; ir (potassium bromide): ν max cm^{-1} 1730, 1680; nmr: δ 2.33 (3H, s, CH_3), 3.92 (3H, s, NCH_3), 6.32 (1H, s, CH).

Anal. Calcd. for $C_{14}H_{12}N_4O_2$: C, 62.68; H, 4.51; N, 20.89. Found: C, 62.61; H, 4.46; N, 21.09.

3-Acetyl-3a,4-dihydro-1,2,5-trioxopyrrolidino[1,2-*a*]quinazoline Hydrazone (**44**).

A mixture of 1 g. of **11**, 0.4 g. of hydrazine hydrate, and 200 ml. of ethanol was refluxed for 12 hours. The solvent was condensed to a small volume, and the resulting precipitate was collected by filtration. Recrystallization from methanol afforded 0.854 g. (81%) of **44** as colorless needles of m.p. > 300°; ir (potassium bromide): ν max cm^{-1} 1715, 1685, 1660; nmr: δ 1.98 (3H, s, $COCH_3$), 3.39 and 5.21 (each 1H, each d, J = 3 Hz, C_3- and C_{3a}-H).

Anal. Calcd. for $C_{13}H_{12}N_4O_3$: C, 57.35; H, 4.44; N, 20.58. Found: C, 57.34; H, 4.56; N, 20.39.

3-Methyl-3b,4-dihydropyrazolo[4,3-*c*]quinazolo[1,2-*a*]pyrrole-5,11-dione (**45**).

A solution of 0.5 g. of **44** in 40 ml. of ethyl cellosolve with the addition of two drops of concentrated hydrochloric acid was treated as described for the preparation of **41** to give 0.28 g. (60%) of **45** as colorless needles

of m.p. > 300°, recrystallized from dimethylformamide; ir (potassium bromide): ν max cm^{-1} 1730, 1650; nmr: δ 2.43 (3H, s, CH_3), 6.31 (1H, s, CH).

Anal. Calcd. for $C_{13}H_{10}N_4O_2$1/5 $(CH_3)_2NCHO$: C, 60.75; H, 4.27; N, 21.88. Found: C, 60.70; H, 3.98; N, 21.77.

3-Acetyl-2-phenylhydrazinopyrrolo[1,2-*a*]benzothiazolin-1-one (**46**).

A mixture of 1.0 g. of **26**, 0.44 g. of phenylhydrazine, and 120 ml. of ethanol was refluxed for 5 hours. After evaporation of the solvent *in vacuo*, the residue was recrystallized from benzene to give 0.546 g. (40%) of **46** as yellow needles of m.p. 193-195°; ir (potassium bromide): ν max cm^{-1} 1700, 1610; nmr: δ 2.32 (3H, s, CH_3), 6.69 (1H, s, CH).

Anal. Calcd. for $C_{18}H_{15}N_3O_2S$: C, 64.09; H, 4.48; N, 12.46. Found: C, 64.20; H, 4.66; N, 12.55.

3-Methyl-2-phenylpyrazolo[4,3-*c*]benzothiazolino[1,2-*a*]pyrrol-10-one (**47**).

A solution of 0.5 g. of **46** in 25 ml. of ethanol with the addition of a drop of concentrated hydrochloric acid was refluxed for 30 minutes. After evaporation of the solvent *in vacuo*, the residue was recrystallized from ethanol to give 0.375 g. (79%) of **47** as colorless needles of m.p. 160-161°; ir (potassium bromide): ν max cm^{-1} 1720; nmr: δ 2.35 (3H, s, CH_3), 7.15 (1H, s, CH).

Anal. Calcd. for $C_{18}H_{13}N_3OS$: C, 67.70; H, 4.11; N, 13.16. Found: C, 67.76; H, 4.25; N, 13.31.

3-Acetyl-1,2-dioxopyrrolidino[1,2-*a*]benzothiazoline Methylhydrazone (**48**).

A mixture of 1 g. of **26**, 0.19 g. of methylhydrazine and 120 ml. of ethanol was refluxed for 6 hours. Evaporation of the solvent left the crystalline residue, which was recrystallized from benzene to give 0.514 g. (46%) of **48** as colorless needles of m.p. 189°; ir (potassium bromide): ν max cm^{-1} 1720; nmr: δ 1.96 (3H, s, $COCH_3$), 2.77 (3H, s, NCH_3), 3.90 and 5.77 (each 1H, each s, C_3- and C_{3a}-H).

Anal. Calcd. for $C_{13}H_{13}N_3O_2S$: C, 56.72; H, 4.76; N, 15.27. Found: C, 56.84; H, 4.79; N, 15.15.

2,3-Dimethylpyrazolo[4,3-*c*]benzothiazolino[1,2-*a*]pyrrol-10-one (**49**).

A solution of 0.275 g. of **48** in 20 ml. of ethanol containing a drop of concentrated hydrochloric acid was treated as described for the preparation of **47** to give 0.163 g. (64%) of **49** as colorless needles of m.p. 170-171°, recrystallized from ethanol; ir (potassium bromide): ν max cm^{-1} 1720; nmr: δ 2.23 (3H, s, CH_3), 3.89 (3H, s, NCH_3), 7.05 (1H, s, CH).

Anal. Calcd. for $C_{13}H_{11}N_3OS$: C, 60.69; H, 4.31; N, 16.34. Found: C, 60.69; H, 4.16; N, 16.43.

3-Acetyl-1,2-dioxopyrrolidino[1,2-*a*]benzothiazoline Hydrazone (**50**).

A mixture of 1 g. of **26**, 0.3 g. of hydrazine hydrate and 200 ml. of ethanol was refluxed for 8 hours. After evaporation of the solvent, the residue was recrystallized from ethanol to give 0.4 g. (38%) of **50** as colorless needles of m.p. 183-185°; ir (potassium bromide): ν max cm^{-1} 1.97 (3H, s, $COCH_3$), 3.84 and 5.75 (each 1H, each s, C_3- and C_{3a}-H).

Anal. Calcd. for $C_{12}H_{11}N_3O_2S$: C, 55.17; H, 4.24; N, 16.09. Found: C, 55.06; H, 4.11; N, 16.27.

3-Methylpyrazolo[4,3-*c*]benzothiazolino[1,2-*a*]pyrrol-10-one (**51**).

A solution of 0.5 g. of **50** in 100 ml. of ethanol containing a drop of concentrated hydrochloric acid was treated as described for the preparation of **49** to give 0.45 g. (97%) of **51** as colorless needles of m.p. 240-242°, recrystallized from ethanol; ir (potassium bromide): ν max cm^{-1} 1710; nmr: δ 2.37 (3H, s, CH_3), 7.10 (1H, s, CH).

Anal. Calcd. for $C_{12}H_9N_3OS$: C, 59.26; H, 3.73; N, 17.28. Found: C, 59.35; H, 3.78; N, 17.12.

1,3-Dimethylpyrazolo[4,3-*c*]benzothiazolino[1,2-*a*]pyrrol-10-one (**52**).

A mixture of 0.5 g. of **51**, 0.5 g. of potassium carbonate and 2 g. of methyl iodide in 100 ml. of acetone was refluxed for 10 hours. After evaporation of the solvent, the residue was dissolved in 70% of ethanol. The insoluble solid was collected by filtration, and recrystallized from methanol to give 0.226 g. (43%) of **52** as colorless needles of m.p. 241-242°; ir (potassium bromide): ν max cm^{-1} 1720; nmr: δ 2.38 (3H, s, CH_3), 3.89 (3H, s, NCH_3), 7.10 (1H, s, CH).

Anal. Calcd. for $C_{13}H_{11}N_3OS$: C, 60.69; H, 4.31; N, 16.34. Found: C, 60.89; H, 4.26; N, 16.24.

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